Objective
To provide internationally comparable data on the frequencies of different causes of death.

Methods
We analysed verbal autopsies obtained during 1999–2002 from 12 demographic surveillance sites in sub-Saharan Africa and Bangladesh to find cause-specific and age-specific mortality rates. The cause-of-death codes used by the sites were harmonized to conform to the ICD-10 system, and summarized with the classification system of the Global Burden of Disease 2000 (Version 2).

Findings
Causes of death in the African sites differ strongly from those in Bangladesh, where there is some evidence of a health transition from communicable to noncommunicable diseases, and little malaria. HIV dominates in causes of mortality in the South African sites, which contrast with those in highly malaria endemic sites elsewhere in sub-Saharan Africa (even in neighbouring Mozambique). The contributions of measles and diarrhoeal diseases to mortality in sub-Saharan Africa are lower than has been previously suggested, while malaria is of relatively greater importance.

Conclusion
The different patterns of mortality we identified may be a result of recent changes in the availability and effectiveness of health interventions against childhood cluster diseases.

Keywords
Mortality/statistics; Cause of death; Statistics; Africa South of the Sahara; Bangladesh (source: MeSH, NLM).

Introduction
Statistics on causes of death are in great demand for developing and implementing public health interventions, but few parts of the world have estimates of cause-specific mortality rates that are reliable enough. This inadequacy is most common in developing countries, where medical personnel are rarely present to record details of deaths, and information on the causes of deaths is usually of poor quality. Because of the absence of reliable information, the overall numbers of deaths and thus, the all-cause mortality rates, are also highly uncertain.

An increasing number of areas in the developing world, especially in Africa, prospectively monitor demographic events, and can thus provide accurate age-specific mortality rates, often for populations of many tens of thousands of people. Many of these Demographic Surveillance Sites (DSS) use verbal autopsy (VA) to assign causes of death. This process involves interviewing family members about the circumstances leading to death, and the symptoms and...
Diverse practices for VA field methodology, coding and analysis have developed in different centres worldwide, which means that the results are hard to compare. The International Network for the continuous Demographic Evaluation of Populations and Their Health (INDEPTH, http://www.indepth-network.org) is trying to standardize VA practices at DSS sites. In collaboration with this effort, we have now recoded VAs from 12 of these centres, mapping them onto the International statistical classification of diseases and related health problems, tenth revision (ICD-10) coding system, and then summarized them according to the categories of the Global Burden of Disease (GBD) study.5 We then calculated age-specific and cause-specific mortality rates. The sites included are in sub-Saharan Africa and Bangladesh.

Our analysis contributes to the evidence base for identifying priorities for health interventions across Africa and in South Asia. It will also provide a baseline for analysis of trends in cause-specific mortality in these regions.

Methods

Study population

At September 2005, INDEPTH had 33 sites undertaking prospective demographic surveillance of populations in developing countries across the world. All INDEPTH sites conducting VAs during 1999–2002 were invited to participate in the study, and VA data and mortality rates were assembled from 12 of these sites. The sites were Agincourt, ACDIS and Manhica in Southern Africa; Butajira, Ifakara, Kisumu and Rufiji in East Africa; Navrongo, Niakhar and Nouna in West Africa; HSID-A and Matlab in Bangladesh.

Demographic surveillance, including continuous recording of births, deaths and migrations, was done in all sites.4 For each site, the time interval for which data were analysed depended on how many data were available.

Calculating mortality rates

Time at risk of disease was calculated for each individual registered in the demographic surveillance system, subtracting periods of absence due to migration. All-cause mortality rates were calculated by dividing the numbers of deaths in an age group by the time at risk, and expressed as deaths per 1000 person-years at risk. We calculated cause-specific death rates for each age group by multiplying all-cause mortality rate by the proportion of deaths assigned to each cause. We did not need to unambiguously assign a single cause to each death. Thus, when coders disagreed on the cause, we analysed the individual codes and used an algorithm to distribute the diagnoses across potential causes. In these instances, we allocated percentages of a death to the codes assigned, in proportion to the number of coders who offered a diagnosis.

When the coders assigned a cause as “unknown”, we counted it as equivalent to no information. For example, if one coder assigned the cause as malaria, another diarrhoea, and a third unknown, the death was allocated as 50% malaria and 50% diarrhoea. When both immediate and underlying causes were assigned, that coder’s assignment was allocated 50:50 between the two codes, so that if the second coder in the previous example assigned the immediate cause as diarrhoea and the underlying cause as malnutrition, the death would then be divided as 50% malaria and 50% diarrhoea and 25% malnutrition.

VAs were done for most of the deaths recorded during the study, but some had too little information for the coders to assign a cause. Where the cause was indeterminate (all coders assigned it as unknown) or where no VA was done, we redistributed the deaths in proportion to the rates estimated from the other VAs (except for those assigned to external causes) for the same age group, year, sex and site. We have not provided confidence intervals for cause-specific mortality rates because this would require assumptions about the distribution of the numbers of deaths. The sample sizes for most sites are substantial, leading to narrow intervals that we have not reported in this paper.

Coding the cause of death

In some sites, just one doctor assigned codes for the cause of death to VAs. In others, two doctors independently coded each VA, and a third coder reconciled disagreement. Other sites obtained codes from three independent doctors. The VA coders generally coded only one cause for each death, usually the immediate cause (i.e. the disease or complication that occurred closest to death). In some sites, the underlying cause was also coded separately. This was defined as the disease or condition that initiated the series of events leading directly to death.

Some coders used the ICD-10 coding system whereas others used local systems. For this analysis, each code used locally (for either the immediate or underlying cause) was translated into an ICD-10 code. This process was checked by the investigators from the sites and revised as necessary. Where multiple codes were assigned for the same death, each of these codes was individually mapped onto ICD-10. The ICD-10 causes of death were then regrouped into the classification used for the GBD study.9

Many sites routinely code deaths due to acute febrile illnesses as malaria, when there is no indication of any other cause. Other sites distinguish deaths
due to malaria from fevers of unknown origin. To harmonize coding across sites, we grouped fevers of unknown origin under malaria for those sites with stable endemic Plasmodium falciparum transmission, but classified such fevers under “other causes” for the remaining sites.

Age standardization
Age-standardized mortality rates were calculated for the major groups of causes, by applying age-specific rates to the INDEPTH standard population. This standardization allowed comparisons between sites that accounted for their different age structures.

Results
Ten of the sites are spread over sub-Saharan Africa, with two sites from Bangladesh (Table 1 (web version only, available at: http://www.who.int/bulletin)). Some of these sites, notably Matlab and Navrongo, have been doing verbal autopsies for a considerable period, although data obtained before 1999 were not analysed in this study. Other sites started verbal autopsy only during the study period of 1999–2003. The data from Butajira were derived from an initial pilot study. The size of the study populations also varied considerably, which affected the number of deaths, and thus, the number of verbal autopsies included in the analyses. Navrongo had the largest number of VAs (8542) because of its high overall death rate, and Matlab had the second largest number (6101) because it had a large population under surveillance.

38 306 deaths were included in the analyses, of which causes were specified for 32 630 (84.9%). The percentage of deaths for which a cause could be assigned varied considerably between sites (Table 1). Excluding the data from Kisumu, where only infant and child mortality was monitored, 17.9% of deaths were in infants, 12.8% in children aged 1–4 years, and 31.8% in people older than 60 years. The percentage of deaths for which causes could be assigned was 86.8% in infants (younger than 1 year) and 83.9% in those older than 60 years.

All the sites show mortality patterns characteristic of rural populations living in poverty. The all-cause mortality rates for the study period were similar to those published previously for the same sites1 with high infant mortality rates (Fig. 1), and high incidences of maternal, perinatal and infectious disease mortality (Table 2, Table 3 and Table 4 (web version only, available from http://www.who.int/bulletin)) in all sites. The most striking differences between them are in the contributions of human immunodeficiency virus (HIV) and malaria.

Although rates of HIV/acquired immune deficiency syndrome (AIDS) are high in all African sites except Butajira and Niakhar, those in South Africa were the highest (Table 2 and Table 3), dwarfing even those in East Africa (Fig. 2). As expected, the age pattern of AIDS diagnosed by verbal autopsies shows clear peaks in young adults and in the youngest children; this contrasts with the
age pattern for tuberculosis (TB), which generally showed an increase in incidence with age (Fig. 2).

Seven of the 12 sites have stable endemic malaria (Table 1), which appears as the most important cause of child mortality in most of Africa, with exceptions being the two South African sites, where it is well controlled, and Butajira in Ethiopia (Table 2). The Butajira site is an area of unstable malaria (both *P. falciparum* and *P. vivax*), with wide variations in transmission intensity associated with variations in altitude.

The malaria rates we have provided for stable endemic areas are inflated by the inclusion of fevers of unknown origin. In the Butajira site, there were few deaths from malaria (0.6 deaths per 1000 person-years), malaria is seasonal and occurs in low-lying areas, and the disease could thus be excluded as a likely cause of most of the deaths from fever (pyrexia) of unknown origin (PUO). The death rate for PUO from Butajira (0.8 per 1000 person-years, included in the category “other”) thus provides an estimate of the true rate of non-malaria PUO mortality in the areas with stable endemic *P. falciparum*. This procedure suggests that there is only a small inflation of the malaria mortality rates in these areas. The two South African sites, which could also be used to provide estimate of non-malaria fever mortality, had negligible numbers of PUO deaths.

Incidence of death attributed to diarrhoeal diseases also varied widely, with the highest proportionate mortality in the West African sites, and the main burden in young children but with high death rates also in the elderly (Fig. 2). In most of the East and Southern African sites, diarrhoeal disease rarely causes death.

Diseases covered by WHO’s Expanded Programme on Immunization (EPI), including measles and those listed as “childhood-cluster” diseases were also most frequent in West Africa but did not often lead to death. In all sites, tropical parasitic diseases (except for malaria) collectively accounted for fewer than 0.05 deaths per 1000 person-years, so these conditions were not taken into account in our calculations.

Economic development is commonly associated with a transition from infectious to noncommunicable diseases. Although neoplasms, diabetes and cardiovascular disease form lesser components of the overall mortality burden in all the sites, there is evidence of health transitions in the Southern African and Bangladeshi sites, with rates for these conditions higher than elsewhere in sub-Saharan Africa (Fig. 3 and Fig. 4). Although Manhica is geographically very close to the South African sites, its mortality patterns are more like those of the East African sites than those in South Africa, with high malaria rates, high maternal mortality, relatively low human immunodeficiency virus (HIV), and low chronic disease mortality. The southern African (including Manhica) and Bangladeshi sites, also have the highest rates of deaths due to injuries (Table 2, Fig. 3 and Fig. 4).

Sites with the highest adult mortality rates, in particular Africa Centre and Butajira, seem to have even worse mortality patterns when age-specific rates are applied to a standard population (Fig. 4). In most of the African sites, noncommunicable diseases are more important when the rates are age-standardized, indicating that a major reason for the low proportions of deaths due to chronic diseases in these populations is the young average age and the low proportion of adults.

**Discussion**

In most sites, death is mainly caused by infectious diseases, with AIDS and malaria particularly frequent, although neoplasms, diabetes, cardiovascular disease and digestive disorders (including in the liver) are also important. There is evidence that South Africa and Bangladesh have high rates of noncommunicable diseases as well as infectious diseases.
On the whole, our results are similar to those of the GBD study,\textsuperscript{9,11} and WHO estimates of the causes of death in children.\textsuperscript{12} But compared with these studies, we recorded a lower contributions of measles in all sites, and lower contributions of diarrhoeal diseases in most sites. Conversely, our estimates of mortality rates caused by malaria in sub-Saharan African sites are higher than those suggested by the GBD study, and the AIDS rates for the South African sites also stand out as much higher than GBD or WHO estimates.

Time trends in cause-specific mortality can explain some of these differences. The WHO estimates were for 1995 for malaria and for 2001 for HIV/AIDS,\textsuperscript{11} but make use of results of epidemiological studies as far back as 1980. During this period, there have generally been an increase in overall trends in child mortality rates in sub-Saharan Africa, but this probably conceals substantial reductions in death from measles as a result of the EPI programme, and in diarrhoeal diseases, as result of oral rehydration therapy. Globally, rehydration therapy has reduced the number of children dying because of severe diarrhoea by as much as two-thirds since it was first introduced in 1979.\textsuperscript{13}

The spread of resistance to antimalarial drugs, especially chloroquine, has almost certainly led to a substantial increase in the numbers of death from malaria,\textsuperscript{14} which along with the HIV/AIDS epidemic, has played a major part in reducing the overall benefits of improvements in health care.

The latest GBD estimates for sub-Saharan Africa are based on a regional model that uses vital registration data from South Africa,\textsuperscript{11} but the contrast between the causes of death in Manhica and those in the nearby South African sites (all three of the southern African sites are within about 300 km of Maputo, and Manhica is nearer to Agincourt than Africa Centre) caution against extrapolations of South African epidemiological data to superficially similar sites elsewhere in sub-Saharan Africa with different environments, ecologies and histories.

Some of the differences between our results and those of the GBD study may also indicate different diagnostic algorithms and their resulting biases. The VA technique assumes that most causes of death have distinct symptom complexes that can be recognized, remembered and reported by lay respondents, and based on this reported information, causes of deaths can be classified into useful categories. The VA method has been validated for both child and adult mortality\textsuperscript{15–18} and results can be adjusted to allow for some of the misclassification biases\textsuperscript{21,22} However, we could assume that the same correction algorithm would be appropriate across multiple sites\textsuperscript{23} and, in the absence of a comprehensive set of validation studies, we could not apply any general corrections for bias to our dataset.

In cases when VAs were incompletely linked with deaths recorded in the demographic database, we analysed all VAs available from the site. This may have led to the inclusion of a few deaths of individuals who were not resident in the area, in particular in the case of the Rufiji DSS, where slightly more VAs were accrued than the number of deaths recorded.

Differences in coding between the sites meant that up to six distinct codes could be assigned for each death in some sites, leading to large numbers codes being assigned, especially in Rufiji and Navrongo.

**Limitations**

The differences between sites in percentages of deaths for which a cause was assigned indicate both differences between sites in coding policies when the cause of death was hard to pinpoint, and also differences in the completeness of follow-up. Our analysis does not distinguish between deaths for which there was no VA and those with a VA coded as uncertain. There are several explanations for the failure to code a death, ranging from the inability to find an individual who knew the deceased to having VA information that was extensive, but difficult to interpret.

Factors influencing the validity of VAs include the type of illness leading to death, characteristics of the dead person, and other factors related to the classification of causes of death, as well as the design and content of questionnaires and field procedures.\textsuperscript{7} Lack of standardization of the procedures can be a serious limitation in comparisons of VA data.\textsuperscript{24} At the time that the VAs that we report were undertaken, little progress had been made in harmonizing procedures for interviewing and coding. Subsequent workshops within the INDEPTH network have achieved some progress, but data accrued with the standardized procedures are not yet available.
Many sites used locally designed coding systems focused on the categories of mortality most relevant to the local research agenda. We achieved a large degree of harmonization in the coding of the VAs by mapping each of these systems onto the ICD-10 codes. A broader classification makes it easier to use the same coding system in a wide range of settings, and though there remain discrepancies between sites in the preferences for different codes, most of these issues do not affect the rates when the causes are further aggregated into the GBD categories. However, much of the variation between sites in the proportion of deaths assigned to the category “other” results from differences in VA methodology, especially in the recording of infrequent causes. The addition of codes for presumptive diagnoses to the ICD system (e.g. “acute febrile illness, presumed due to malaria”), would greatly facilitate standardized coding of VAs, and allow analysis of narrower categories of mortality.

The procedure of redistributing deaths of unknown cause proportionately to the other causes eliminates some of the inconsistencies between sites that arise from different procedures for arriving at a consensus diagnosis from multiple coders. An alternative to our procedure is to include an additional category of indeterminate deaths, as in the WHO estimates of causes of death in children, an approach that recognizes that some causes (such as degenerative diseases in the elderly) are inherently harder to code than others (e.g. accidents and violence). However, in an unknown fraction of cases, the absence of etiological information resulted not from diagnostic problems, but rather from failure to locate relatives willing to give verbal autopsies, or from only very little information being provided. The reasons for lack of information may therefore be unrelated to the actual cause of death, thus justifying the assumption that these causes come from the same distribution as those of the other deaths.

The sites are not a random sample of areas within the countries represented, nor do they include urban areas. A thorough analysis of representativeness would involve comparison of all-cause mortality rates with those estimated from Demographic and Health Surveys, and lies outside the scope of this paper. Demographic surveillance was initiated in each site for different reasons, but in each case to provide epidemiological information for the wider social and ecological zone in which it is found. Some of the differences between sites clearly reflect differences in procedures, for example the high proportion of unclassifiable deaths in Agincourt was probably a result of the local operating procedures used by the coders. Child malnutrition, which is related to many deaths attributed to other causes, contributed to many deaths in Kisumu, but this high frequency could also reflect local coding preferences for multicausal deaths. A comparison of nutritional indices between sites would help to indicate whether there are real epidemiological differences. Other differences, such as the high rates of neonatal mortality in Kisumu, are difficult to explain other than as a true epidemiological occurrence.

**Malaria**

In areas of stable endemic malaria (in seven sites), coders assumed that deaths associated with acute febrile illness were due to malaria, unless there was strong evidence for an alternative cause. For consistency, we allocated deaths assigned to fevers of unknown origin as being caused by malaria in all sites with endemic *P. falciparum*. Although this process might seem likely to exaggerate the effect of malaria, assignment of malaria deaths by verbal autopsy has a sensitivity less than 100%, as well as imperfect specificity. Since death from fever of unknown origin in both Burujitra and South Africa is infrequent, it is unlikely that our assumption introduced any significant bias into child mortality rates. It seems likely though that many, if not most, deaths in the over 45-year age group coded as malaria were caused by other febrile illnesses. *P. falciparum* malaria is over-diagnosed in adults in endemic areas.

**HIV/AIDS**

HIV-related deaths are often associated with TB, which introduces a further element of uncertainty about the cause of death. In Matlab, HIV prevalence is low and TB was recognized as a major cause of death before the HIV epidemic. In such situations, it is unlikely that many TB deaths were related to underlying HIV infection. But in the Africa Centre, HIV testing is integrated into local research programmes, meaning that HIV status could be determined. In most of the other African sites, the proportion of the TB deaths with underlying HIV remains unclear. However, the different age trends for AIDS and TB mortality show that VA coders do distinguish these etiologies even in areas of high endemicity of both infections.

Many deaths are clearly multifactorial, and can involve several medical conditions. Some factors such as under-nutrition are recognized as important underlying causes of many deaths associated with infectious diseases, but are likely to appear in VAs in only the most clear-cut cases. Other forms of co-morbidity are under-researched but may well be involved in many deaths. The effect of such causes is better measured by prospective studies of the overall impact of the risk factor on all-cause mortality. Data on the cause of death thus has a role in the assessment of the numbers of deaths that can be averted by specific interventions, such as antismoking campaigns or integrated management of childhood infections (IMCI), but we caution against inferring mortality amenable to health care directly from cause-specific rates.

Our estimates of cause-specific mortality rates should influence resource allocation within international health agencies. They should also prove a valuable contribution to the evidence base for identifying health intervention priorities across Africa and in South Asia. Our results will also form a baseline for analysis of trends in cause-specific mortality over time, both in the context of interventions within the INDEPTH sites and across the regions represented by these centres. Demographic surveillance and verbal autopsy programmes continue in these sites and will in future provide further data, directly comparable with this baseline, with which to evaluate trends in cause specific mortality.

**Competing interests:** none declared.
Résumé

Taux de mortalité par cause en Afrique subsaharienne et au Bangladesh

Objectif Fournir des données comparables au niveau international sur la fréquence des différentes causes de décès.

Méthodes Il s’agissait d’analyser les autopsies verbales transmises entre 1999 et 2002 par 12 sites de surveillance démographique en Afrique subsaharienne et au Bangladesh afin de déterminer les taux de mortalité par cause et par âge. Les codes affectés aux causes de mortalité utilisés par les sites ont été harmonisés pour être conformes au système de la CIM10 et récapitulés selon le système de catégorisation de la charge de morbidité mondiale 2000 (version 2).

Résultats Les causes de décès dans les sites africains sont très différentes de celles relevées au Bangladesh, où certains éléments indiquent une évolution de la morbidité des maladies transmissibles aux maladies non transmissibles et où le paludisme est peu présent. Le VIH est en revanche la cause dominante de mortalité dans les sites sud-africains à la différence de ce que l’on observe dans les sites à forte endémie palustre des autres pays d’Afrique subsaharienne (même au Mozambique voisin). Les contributions à la mortalité de la rougeole et des maladies diarrhéiques sont moins élevées en Afrique subsaharienne qu’on ne le pensait précédemment, alors que le paludisme revêt une importance relativement plus grande.

Conclusion Les différents schémas de mortalité mis en évidence résultent peut-être d’une modification récente de la disponibilité et de l’efficacité des interventions sanitaires contre les maladies de l’enfant apparaissant en grappes.

Resumen

Tasas de mortalidad por causas específicas en el África subsahariana y en Bangladesh

Objetivo Aportar datos comparables internacionalmente sobre la frecuencia de las distintas causas de defunción.

Métodos Analizamos las autopsias verbales obtenidas durante 1999–2002 en 12 sitios de vigilancia demográfica del África subsahariana y de Bangladesh a fin de determinar las tasas de mortalidad por causas y por edades. Los códigos de las causas de defunción utilizados por los distintos sitios fueron armonizados con arreglo al sistema de la CIE-10, y resumidos mediante el sistema de clasificación de la Carga Mundial de Morbilidad 2000 (versión 2).

Resultados Las causas de defunción en África difieren marcadamente de las observadas en Bangladesh, donde los datos sugieren una transición sanitaria hacia las enfermedades no transmisibles, con pocos casos de malaria. La infección por VIH destaca entre las causas de mortalidad en los lugares de Sudáfrica analizados, que contrastan con las causas observadas en los lugares de alta endemia de malaria del resto del África subsahariana (incluso en el vecino Mozambique). La contribución del sarampión y de las enfermedades diarreicas a la mortalidad en el África subsahariana es inferior a la sugerida hasta ahora, mientras que la malaria tiene una importancia relativamente mayor.

Conclusión Los diferentes perfiles de mortalidad que hemos observado podrían ser el resultado de los últimos cambios experimentados por la disponibilidad y la eficacia de las intervenciones sanitarias contra las enfermedades infecciosas infantiles más comunes.

Melhus

معدلات الوفيات الخاصة وأسباب معينة في البلدان الواقعة جنوب الصحراء الأفريقية وفي بغلاديش

هدف: تقديم معلومات يمكن مقارنتها على الصعيد الدولي حول تكرار الأسباب المتقطعة للوفيات.

الطريقة: قمنا بتحليل نمط التشريky الافتراضي إلى حصلنا عليه خلال الأعوام 1999 - 2002 من 12 موقعًا برغوريًا في جميع البلدان الواقعة جنوب الصحراء الأفريقية وفي بغلاديش بفترة معدلات الوفيات الخاصة بأشياء معينة، وخاصة الأمراض برضى معينة، وقد تم تسجيل الانضمام بين الروماتيزم الخاص وأسباب الوفيات المستخدمة في تلك الواقعة تستند على نظام المراجعة العاشرة للتصنيف الدولي للأمراض. مع تحليلها ضمن نظام التصنيف الخاص بالعمل، العالمي للأمراض في إرساء أحدث نظام أطول.

الاستنتاج: إن أسباب الوفيات في إفريقيا تختلف كثيرًا عن ما هي عليه في
References


